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Clustering Analysis for Sorting ATP-Induced Nociceptive Firing in rat Meninges

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Abstract

© 2016, Springer Science+Business Media New York.We previously reported the pronociceptive effect of extracellular ATP on meningeal branches of the trigeminal nerve. Based on this, we proposed ATP-driven purinergic mechanisms as important contributors to migraine pain. However, the neurochemical profile of the single nociceptive fibers composing the trigeminal nerve remained unsolved. Here, we present a clustering approach to separate and characterize ATP-induced nociceptive spikes obtained from the trigeminal nerve using a suction electrode. By combining a number of procedures to ensure adequate separation of spikes into clearly distinguishable clusters, we were able to reconstruct single fiber activity, which was characterized by a uniformity of spike shapes and specific signatures of the autocorrelation function. This allows us to reveal, at single fiber level, the sustained time-course of responses to ATP and their respective firing frequencies. These firing frequencies predicted the temporal summation of pain signals in the brainstem and spinal cord. Our findings contribute to a better understanding of the peripheral purinergic mechanisms of trigeminal pain, including migraine pain, and suggest a novel reliable approach for testing other pronociceptive agents potently implicated in migraine.

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Keywords

ATP, Cluster analysis, Migraine, Pain, Patch clamp, Trigeminal neuron